Secondary Cutaneous Mantle Cell Lymphoma

ABSTRACT

Mantle cell lymphoma is a rare form of B-cell non-Hodgkin's lymphoma that presents as a low-grade lymphoma and has a different prognosis than other types of lymphoma. Mantle cell lymphoma is an aggressive tumor that can manifest as nonspecific symptoms, such as nasal obstruction, dyspnea, and erythematous indurated cutaneous plaques. Diagnosis can be established with confidence using immunohistochemistry. In this report, a case of nasopharyngeal mantle cell lymphoma metastasizing to the skin is discussed.

KEY WORDS: Lymphoma, mantle lymphoma, metastasis, tumor

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Lymphomas are a heterogeneous group of neoplasms displaying varied clinical and morphological characteristics, usually classified as Hodgkin's and non-Hodgkin's lymphoma (NHL). NHL is further stratified according to the cell of origin as either B-cell or T-cell type. Skin manifestations in lymphomas could be primary or secondary to a primary nodal lymphoma. Primary T-cell NHLs commonly affect the skin, whereas primary B-cell NHLs are more common in the lymph nodes.[1] Although all lymphomas including mantle cell lymphoma (MCL) can metastasize to the skin, secondary involvement of the skin is uncommon and indicates a poor prognosis.[2] Here, we describe the case of a patient presenting with extensive nodules and plaques on the skin with MCL.

CASE REPORT

A 50-year-old woman presented with a sudden onset of multiple reddish nodules over the face, neck, trunk, and upper limbs three weeks prior to presenting to our clinic. The patient reported simultaneous bilateral nasal obstruction due to a nasopharyngeal mass for which she underwent a biopsy. A history of anorexia and significant weight loss was present. Examination revealed massive, hard, and nontender cervical, axillary, and inguinal lymphadenopathy, as well as hepatosplenomegaly and diffuse infiltration of the palate, nasal septum, turbinates, and posterior pharyngeal wall.

Cutaneous examination revealed diffuse infiltration of the face and ears along with multiple hard, nontender, skin colored erythematous papules and nodules coalescing to form plaques over the neck, trunk, and upper limbs (Figure 1). The differential diagnoses of metastatic cutaneous deposits from a primary nasopharyngeal carcinoma and cutaneous lymphoma were considered and a skin biopsy was taken. Routine blood investigations revealed anemia (hemoglobin: 8.4gm%), leukocytosis (16,800/µL), and absolute lymphocytosis (77% including atypical lymphocytes). Biochemical investigations were within the normal limits. Urine analysis for Bence Jones proteins was negative and urine routine examination findings were within normal limits. Chest radiogram was normal. Ultrasound abdomen showed hepatosplenomegaly and abdominal lymphadenopathy.

The histopathology of nasopharyngeal biopsy revealed low-grade non-Hodgkin's lymphoma. Fine-needle aspiration cytology from cervical lymph nodes showed a scattered, monomorphic population of atypical lymphoid cells with high nuclear-cytoplasmic (N:C) ratio, and a few conspicuous nucleoli and atypical mitotic figures. Histopathological evaluation of skin biopsy showed diffuse sheets composed of uniform, small, atypical lymphoid cells with irregular nuclei, condensed chromatin, and scant cytoplasm without any

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proliferation centers. The papillary dermis was characteristically spared (Grenz zone) (Figure 2). A panel of immunostains composed of cytokeratin, leukocyte common antigen, cluster of differentiation (CD)3, CD5, CD10, CD20, CD23, and cyclin D1 was employed. The tumor cells were negative for CD3, CD10, and CD23 while being positive for leukocyte common antigen, CD5, CD20, and cyclin D1 (Figure 3), which confirmed the diagnosis of NHL, B-cell type (MCL). Bone marrow biopsy showed hypercellular marrow spaces (cellularity 85%–90%) showing infiltration by sheets of atypical lymphoid cells. The final diagnosis of a secondary cutaneous (B-cell NHL) presentation arising out of primary nasopharyngeal MCL NHL along with bone marrow infiltration was made. The patient was started on chemotherapy but was lost to follow-up.

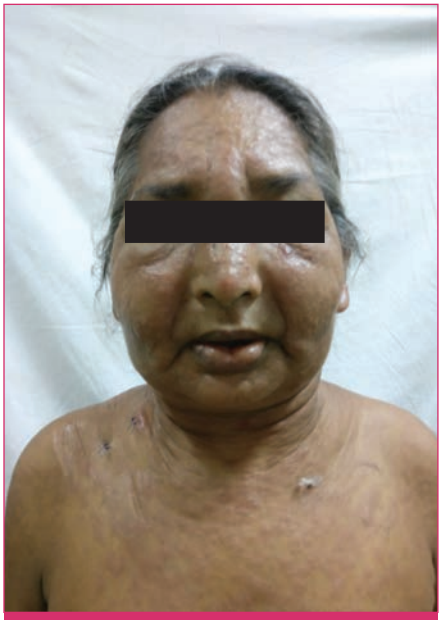

FIGURE 1. Case of secondary cutaneous MCL with multiple erythematous papulonodular lesions and diffuse indurated sclerodermatous skin

DISCUSSION

MCL, derived from the B-cells in the mantle area of the lymphoid follicles, is a clinically distinct rare form of nodal NHL. MCL, affecting 3 to 10 percent of all patients with T- and B-cell NHL, is an aggressive lymphoid malignancy previously considered to be a low-grade lymphoma.[2] It invariably presents systemically at an advanced stage with secondary extranodal involvement of the gastrointestinal tract, Waldeyer's ring, bone marrow, liver, lung, central nervous system, skin, and other organs.[3]

Primary cutaneous MCL is quite rare and occurs only in 2 to 6 percent of patients. Secondary cutaneous involvement in MCL occurs in 17 percent and is usually observed late in the course of disease (Stage 4).[2] Primary and secondary cutaneous lymphomas are identical in clinical morphology but are prognostically different. The primary type tends to remain in the skin only, having an indolent course and a good prognosis relative to the secondary type, which often presents with a multifocal involvement and portends a poor prognosis.[4] The latter could be due to direct infiltration of the skin by lymphoid cells (specific) or due to a paraneoplastic phenomenon (nonspecific), which occurs as a result of immune dysregulation caused by the lymphoma, leading to an increased incidence of autoimmune phenomena like paraneoplastic pemphigus, granuloma annulare, and Sjögren's syndrome.[4]

Histopathologically, MCL comprises the monotonous proliferation of small- to medium-sized lymphoid cells with scant cytoplasm, irregular cleaved nuclei with coarse chromatin, and inconspicuous nucleoli and a zone of sparing (Grenz zone) in the papillary dermis.[2] This Grenz zone differentiates B- from T-cell lymphomas, as the latter do not have any such zone of sparing, but rather show epidermotropism.[1] The irregularity of nuclear contour and the lack of proliferation centers further differentiates MCL from another variant of NHL like small lymphocytic lymphoma or chronic lymphocytic leukemia, which is often regarded as its close histopathological differential diagnosis.[3]

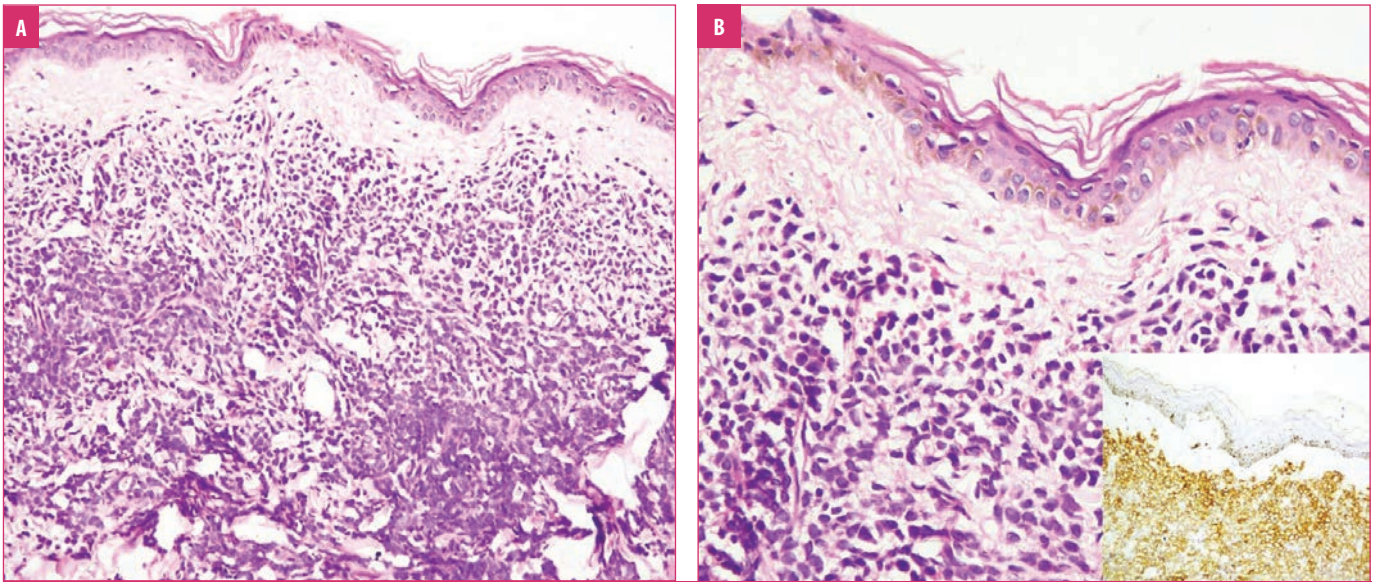

FIGURE 2. Secondary cutaneous MCL—**A)** Photomicrograph shows diffuse dermal cellular infiltrate composed of monotonous/monomorphic uniform small lymphocytes with round hyperchromatic nuclei, inconspicuous nucleoli, and barely discernible cytoplasm with typical sparing of the papillary dermis (Grenz zone) (hematoxylin and eosin ×400); **B)** high-power microscopy shows the Grenz zone above sheets of small lymphocytes with round hyperchromatic nuclei, inconspicuous nucleoli, and barely discernible cytoplasm (hematoxylin and eosin ×400); the inset shows CD20 expression by malignant cells; the sample was negative for CD3, CD10, and CD23 expression (immunohistochemistry ×400).

Immunohistochemically, strong CD20 positivity along with cyclin D-1 positivity combined with CD10 and CD23 negativity differentiates MCL from all other lymphomas.[3] Cyclin D1 positivity is quite specific for MCL; however, it can be positive in a few cases of hairy cell leukemia or splenic lymphoma with villous lymphocytes.[8] The pathogenesis of MCL involves the activation of the *PRAD 1* gene by translocating the long arm of chromosome 11 to chromosome 14, leading to increased cell turnover due to the overexpression of cyclin D1.[5]

More than 45 patients with cutaneous MCL have been described in the literature as single case reports. Most of the patients who have been reported on had cutaneous MCL secondary to the lymph nodes or bone marrow. Some patients showed involvement of the spleen, lung, central nervous system, and gastrointestinal tract.[5] There have also been isolated reports of involvement of the bronchus, buccal mucosa, hard palate, and lingual tonsils.[6]

Men are more commonly affected than women, with a male-to-female ratio of 13:4. The median age for diagnosis is 62.5 years.[5] Eighty percent of the patients are in Stage 3 or 4 disease and 70 percent have bone marrow invasion at the time of diagnosis. Trunk (60%), face (30%), arm (20%), thigh, leg, and scalp are the commonly reported sites.[7] To the best of our knowledge, only three cases of MCL involving the nasopharynx have been described.[8–10] However, none of these cases had cutaneous involvement. This makes the present case the first such case to present with nasopharyngeal obstruction and, later, the development of cutaneous metastasis and dissemination.

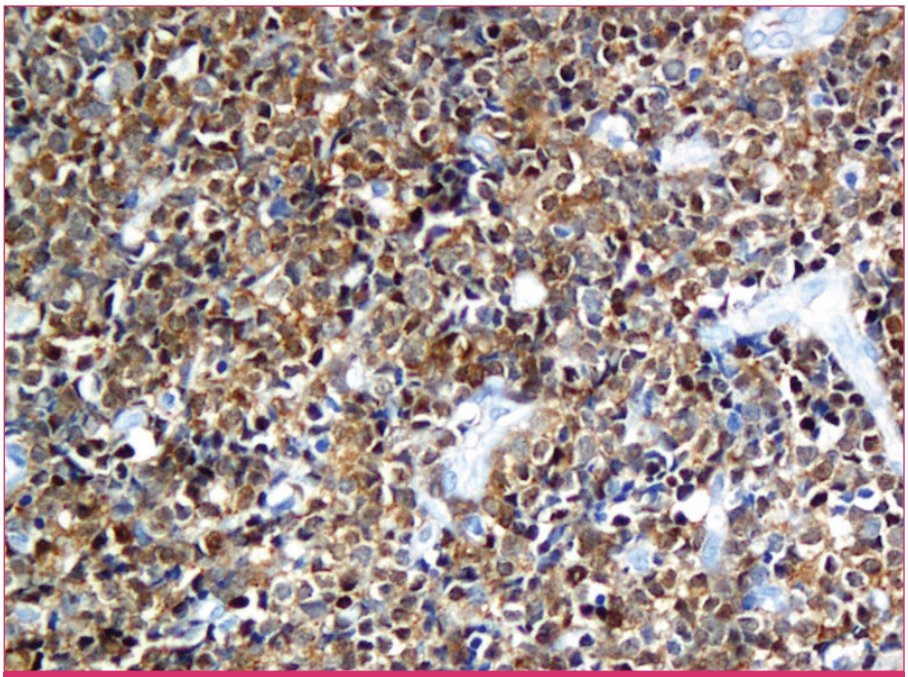

FIGURE 3. Secondary cutaneous MCL—Cyclin D1-positive lymphoid cells shows nuclear positivity on immunostaining (immunohistochemistry x400).

SUMMARY

It is difficult to diagnose MCL in the skin because it morphologically and histopathologically mimics many other indolent lymphomas and pseudolymphomas. Standard chemotherapies being adopted for the treatment of other small lymphoid malignancies have led to unfavorable results in MCL.[3] It is important to consider that this aggressive tumor can also present initially as nasal obstruction and dyspnea.[8,10] Thus, the careful and early immunohistochemistry of tissues taken from the nose and oral cavity for any tumor obstructing these pathways is often rewarding. It is pertinent to mention here that all cutaneous lymphomas should undergo immunohistochemical studies, especially cyclin D1 staining, to confirm MCL as it apparently looks benign but has an aggressive course and bad prognosis, warranting the early institution of aggressive therapy.

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